Letter to the Editor

reprinted from THE LANCET, *February* 24, 1951, *p.* 473

METHONIUM COMPOUNDS IN HYPERTENSION

SIR,—After Kay and Smith [1] observed that the potency of the halide salts of hexamethonium given orally, expressed in terms of the cation, was highest for the iodide and lowest for the chloride, with the bromide intermediate, clinical studies of this drug have been made mostly with the bromide or iodide. It seems improbable, however, that the halide anion of such a salt, which must be completely dissociated in solution, can exert any significant effect on the activity of the hexamethonium cation, or even on its absorption. In view of the possibilities of bromism [2] and of iodism from the use of the bromide or iodide, we have been prompted to test the purity of some of the available preparations in order to determine whether the reputed inefficacy of the chloride was associated with any impurity ; and to verify whether, with pure salts, the biological activity of the cation did indeed vary with the different halide ions. We have determined the halide content of samples of hexamethonium salts, and have assayed biological activity, using the antagonism of hexamethonium to the action of acetylcholine on the frog's rectus abdominis (limits of error 7–10%, P = 0·05). The results were as follows :

Hexamethonium salt	*Biological activity*	*Halide content (% theoretical)*
1. Iodide . .	93	94
2. Iodide . .	100	99
3. Iodide . .	100	100
4. Bromide	90	94
5. Bromide	100	99
6. Chloride	80	84
7. Chloride	97	99

Biological potency is given (in terms of the cation) as percentage of that of the pure iodide (Salts 2 and 3).

It will be seen that biologically several of the salts were below theoretical potency, and that in each case

1. Kay, A. W., Smith, A. N. *Brit. med. J.* 1950, ii, 807.
2. Rosenheim, M. L. *Lancet*, Feb. 10, 1951, p. 347. Holt, M. C., Litchfield, J. W. *Ibid.*

there was evidence of impurity. One particular cause of apparent inefficacy of the chloride came to our attention. We obtained a sample of chloride which had been made up as a powder in a waxed paper, in which it had remained for some months. On opening the paper no powder could be seen ; but simple extraction of the paper with saline, followed by biological assay, produced 91% of the quantity of hexamethonium stated to be within the paper. The chloride, therefore, is sufficiently hygroscopic to take up so much water-vapour that it can go into solution and impregnate the wrapping-paper.

We believe, therefore, that the results of Kay and Smith may have been due to a failure to give the full dose intended, because of some impurity in the chloride used—probably water. We suggest that the chloride, offering as it does freedom from actions other than those of the hexamethonium cation, should be more fully tested therapeutically. The compound should be issued in a form in which it is not liable to absorb moisture, leading to errors in dosage.

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